Management of Midline Facial Clefts

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Abstract Median or midline facial clefts are rare anomalies of developmental origin, etiology of whose occurrence is still unknown precisely. The most basic presentation of midline facial clefts is in the form of a Median cleft lip which is defined as any congenital vertical cleft through the centre of the upper lip. First described by Bechard in 1823, it is the most common amongst all atypical clefts reported. The incidence is about 1:10,00,000 births. This may occur as a sporadic event or as a part of an inherited sequence of anomalies. It arises embryologically from incomplete fusion of the medial nasal prominences. The authors present a series of eight cases with varying degrees of midline facial clefts. This review article aims to give a broad idea on the various classifications used for further understanding of midline facial clefts and a brief idea about the various surgical management techniques used in the repair of these facial clefts.

Keywords Midline cleft lip · Triangular flap · Z-plasty · Midline facial cleft

Introduction

Midline facial clefts are uncommon facial deformities, the genetics of which are unknown. A median or midline cleft lip has been broadly defined as any congenital vertical cleft through the centre of the upper lip [1]. It was first described by Bechard in 1823. It arises embryologically from incomplete merging of the medial nasal prominences, which form the intermaxillary segment. Of all the patients with cleft lip and palate, the incidence of median cleft lip has been placed between 0.43 and 0.73 % [2]. When the more common forms of unilateral and bilateral clefts of the lip and palate are eliminated, the incidence of atypical clefts has been estimated as low as 1 per 100,000. Of these, the median facial cleft is by far the most common [3].

Although various causative factors have been suggested, the exact cause of the occurrence of a median cleft lip is still unknown. As with other clefts, there is a clear association between common teratogenic substances such as alcohol and drugs used during fetal development [4].

Paul Tessier presented the classification of craniofacial clefts which were numbered 0–14 in clockwise system with orbit serving as the axis. In Tessier 0 through 14 the median or midline clefting can vary from simple central vermillion notch to a very wide cleft along with hypertelorism and bifid nose [5].

Midline clefts of face can be subdivided into two major categories: the first group has signs of hypoplasia or agenesis of midline craniofacial structures and amentia. The second group which does not affect the intelligence is of a milder variety. In comparison to other facial clefts; median

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facial clefts are rarely associated with extracranial abnormalities [4].

In 1998, Kawamoto and Patel reviewed the six largest published studies of typical and atypical clefts [3, 6–8]. Their review supported the relative frequency of median clefts when compared with oblique clefts.

Ortiz-monasterio reviewed 6500 craniofacial clefts treated over a 20 year period. Of the 345 atypical clefts found in 176 patients, 92(66.7 %) had median clefts corresponding to a Tessier 0 classification [9].

The fragmentation of literature on midline cleft has led to substantial variations in management. This article intends to broadly review the pathomorphogenesis, diagnosis and classification of median facial clefts. In addition treatment variations are discussed for this relatively rare entity.

Developmental Pathogenesis

Development of lip and palate is a very complex series of events which require a very high degree of coordination and precise timing of cellular migration, growth and differentiation. In the 4th week of intra-uterine life, migration of neural crest cells through the mesenchymal tissue into the developing craniofacial region takes place. These neural crest cells participate in formation of frontonasal eminence, the paired maxillary process and paired mandibular process. Formation of the nasal placodes (ectodermal thickenings) takes place in the 4th week and divides the lower portion of frontonasal prominence into paired medial and lateral nasal process. By the end of the 6th week of development, merging of the medial nasal processes with one another and with the maxillary processes on each side leads to formation of the upper lip and the primary palate. Immediately before completion of these processes, the lateral nasal process has a peak of cell division that renders it susceptible to teratogenic insults, and any disturbance in growth at this critical time can lead to failure of the closure mechanism [10].

The development of facial clefts on embryological level has been proposed and explained by different theories. The two most prevailing theories are the theory of lack of fusion by Dursy [11] and His [12] and the theory of mesodermal migration by Pohlman [13], Veau [14], Warbrick [15] and Stark [16].

Dursy in 1869 postulated that clefts form as a result of failure of fusion of defined facial elements. The complete formation of the upper lip will be dependent on the normal fusion of the medial nasal prominence, lateral prominence and the medial aspect of maxillary process. According to Fusion theory, an arrest of merging of any of these processes can lead to a cleft.

The theory of mesodermal penetration was presented in 1910 [13]. According to this theory clefts result from a failure of mesodermal penetration. The developmental areas are not specific junctions; but instead composed of continuous bilamellar ectodermal membranes with focal regions where mesoderm acts to contour the merging of embryologic process.

In 1983, four primary sites of cleft formation were identified by Vermiej-Keevs et al. [17] between:

1. The junction of medial and lateral processes and the maxillary process
2. The lateral nasal and maxillary processes
3. The maxillary and mandibular processes and
4. The palatine processes

The closure of the ectoderm at these junctions occurs by the 17 mm crown-rump (CR) length stage, which corresponds to 7th gestational week. True clefts occur when the epithelial merging at the aforementioned sites are disturbed before the 17 mm CR length period. Dysplasia, false or pseudoclefts occur when the disruption occurs after the 17 mm CR stage because of interference to the multiple ossification centres that form the facial skeleton [18].

Sulik [19] explained atypical clefts by the variability in the location of the ossification centres. He postulated that more common Tessier clefts are formed at the seam of two minor ossification centres. In case of Tessier 0–14 clefts, the disruption of smaller growth centre units within the nasofrontal process contribute to the formation of a midline cleft.

Carsten's [20] Neuromeric Theory of Embryological Development described the development of craniofacial clefts on the basis of embryological development of neuroanatomy. According to this theory, embryonic neural crest cells arising from each neuromere induce development of nerves and concomitant arteries and support the development of specific craniofacial tissues or developmental fields. Abnormalities in one field can affect the shape and position of developing adjacent fields. Craniofacial clefts represent states of excess or deficiency within and between specific developmental fields. Tessier's observational cleft classification system can be re-defined using neuroanatomic embryology. Reassessment of Tessier's empiric observations demonstrates a more rational rearrangement of cleft zones, particularly near the midline.

Molecular studies have shown that initiation and outgrowth of the facial processes and specification of their identity is partly controlled by interaction of fibroblast growth factors, Sonic hedgehog (SHH), Bone morphogenic proteins, the homeobox containing genes, Barx 1 and Msx 1, the distal less homeobox containing genes (Dlx) and local retinoic acid gradients [21, 22].

Midline facial clefts can come in the entire spectrum, ranging from a simple vermilion notch to the more severe lesions with rhinoschisis and hypertelorism.

Classification

The median cerebrofacial clefts can be expressed as a wide spectrum and this variability accounts for the lack of a single accepted precise classification. In 1963, DeMyer and Zeman [23] defined the term holoprosencephaly and thus initiated the most well known classification of midline facial clefts based on the underlying morphology of the brain (Table 1).

They suggested that there is a strong correlation that exists between the severity of the facial dysmorphology and the development of the forebrain. The median facial anomalies are broadly separated into those with a deficiency of tissue and those with a normal or excessive amount of tissue. Those in the former group ranged from the most severe type, cyclopia (Type I), to patients with minor hypoteleorbitism, flattened nose, and a bilateral cleft lip (Type V). This scheme was modified by Cohen [24] and subsequently by Elias, Wilson, and Kawamoto (Table 2).

The first three groups of this system are identical to DeMyer's. However, Groups IV through VI separated those individuals with semilobar brain morphology from those with a lobar configuration. In addition, a category is developed to include those with a normal brain combined with hypoteleorbitism, a flattened nose, and the presence or absence of a false median cleft. The purpose of this classification is to provide the surgeon with a guideline for predicting life expectancy. Hence a decision whether to operate or not can be taken in a more reasonable way.

DeMyer's second broad category of near normal or excess tissue was termed median cleft face syndrome. Although this term is frequently cited in the literature, the appearance of these findings is not truly a syndrome. Sedano et al. [25]

suggested the term frontonasal dysplasia as more accurate language, but this term does not include the important cleft of the median lip. Kawamoto and Patel [3] preferred the term median cleft face dysmorphism to describe the assemblage of features that represent this entity. Regardless of the terminology, these cases include varying degrees of hypertelorbitism, V-shaped frontal hairline, bifid cranium, median cleft of the upper lip, median cleft of the premaxilla, median cleft of the palate, and primary telecanthus. Unlike the holoprosencephaly classification, this group of facial anomalies is less reliable as predictors of the underlying brain morphology.

Materials and Method

The patients were of age groups 1–35 years. The total number of patients were 8 in the study group which presented to our center between September 2008 and May 2013 (Table 3).

All patients underwent thorough medical examination followed by routine investigations as well as CT scans in required cases. Cases with a rather larger deformity involving the entire Craniofacial Complex were excluded. The surgery was done only for cases with isolated clefts of upper lip. All the patients who were operated upon were mentally stable and were evaluated by a pediatrician and a medicine specialist. The midline cleft defects may be associated with other defects the severity of which might dictate the urgency and sequencing of repair of midline clefts. Hence the prioritization sequence and plan for surgery was customised as per the need of the patient and need for a further procedure was planned.

Surgical Technique

All the cases of midline cleft lip were operated under general anesthesia with oral intubation. The surgical

Table 1 Holoprosencephaly (DeMyer [23], Cohen et al. [24])

Type or group	Facial morphology	Brain morphology
I. Cyclopia	Monophthalmia, synophthalmia, or anophthalmia Proboscis (single/double), arhinia	Alobar
II. Ethmocephaly	Extreme hypoteleorbitism Proboscis (single/double), arhinia	Alobar
III. Cebocephaly	Hypoteleorbitism Proboscis type nose (blind end/single nostril)	Alobar
IV.	Hypoteleorbitism Flat nose Median cleft lip	Alobar (usually)
V.	Hypoteleorbitism Flat nose Bilateral cleft lip	Semilobar or lobar

Table 2 Median cerebrofacial dysmorphogenesis (after Kawamoto and Patel [3])

Type or group	Facial morphology	Brain morphology	Operative procedure <i>Holoprosencephaly</i>
I. Cyclopia	Median monophthalmia, synophthalmia, or anophthalmia Proboscis (single/double), arhinia	Alobar	None
II. Ethmocephaly	Extreme hypoteleorbitism Proboscis (single/double), arhinia	Alobar	None
III. Cebocephaly	Hypoteleorbitism Proboscis type nose (blind end/single nostril)	Alobar	None
IV.	Hypoteleorbitism Flat nose False median cleft lip	Alobar/semilobar	None
V.	Hypoteleorbitism Flat nose False median cleft lip	Lobar	Lip/palate repair
VI.	Hypoteleorbitism	Normal	Lip/palate repair
VIa.	Flat nose		LeFort III/facial bipartition
VIb.	False median cleft lip No false median cleft lip		

Modified from Elias et al. (1992)

Table 3 Cases between Sep 2008–May 2013

S. no	Gender	Age (years)	Diagnosis	Associated anomalies	Treatment done
1.	Male	6	Midline cleft lip	Bifid tongue, hypertelorism, alveolar notching, mentally challenged	Lip repair
2.	Female	1	Midline cleft lip	None	Lip repair
3.	Male	30	Midline cleft lip	Cleft of soft palate, lip	Lip repair
4.	Female	26	Midline cleft lip	Mentally challenged	Lip repair
5.	Male	11	Midline cleft lip and alveolus	Bifid nose, hypertelorism, premaxillary agenesis, absence of corpus callosum, mental status—normal	None
6.	Female	13	Midline cleft lip(vermillion only)	Bifid nose, hypertelorism, coloboma (R) eye	Nose repair, lip repair
7.	Female	4 months	Midline cleft		Lip repair
8.	Female	4 days	Midline cleft	Premaxillary agenesis	None

incision was outlined with an inverted ‘V’ fashion (Fig. 1). Through the incision, the midline fibrotic decussation of the orbicularis oris could be seen. Some of its muscular fibers were aberrantly inserted obliquely toward the nasal sill and superficially into the median cleft deformity of the skin. Dissection on superficial and deep aspect of the orbicularis oris was extended laterally 1.5 cm on either side of the midline. Separation was continued cephalad to free the abnormal muscular attachments from the base of the nose. The median fibrotic band was excised completely and the free ends of the muscles were then approximated. The release of the frenular attachment in combination with advancement of tissue by V–Y closure immediately restored a normal appearance to the tubercle. Recovery was uneventful, and a good postoperative contour of both the

philtrum and lip vermillion, at rest and with animation, was achieved (Figs. 2, 3).

Discussion

The rarity of occurrence and the vast diversity of presentations of the median facial clefts of the upper lip is responsible for the relative paucity of literature, discussing the presentation, pathogenesis and surgical management of this congenital malformation.

The developmental error that results in midline facial defects usually occurs during the third week of gestation. At this time bilateral thickening of the frontonasal process, termed olfactory placodes, appear on the primitive forebrain.

Fig. 1 Incision marking in an inverted 'V' fashion

Fig. 2 Preoperative view of midline cleft lip

Fig. 3 Postoperative view of midline cleft lip

These thickenings of the surface ectoderm become the medial and lateral nasal prominences that contribute to the formation of the nasal philtrum and upper lip. Fusion of the globular process is responsible for the formation of the anterior portion of the hard palate, the central dentoalveolar ridge, and the central upper lip and philtrum. It is essential that fusion of these prominences occur for normal development of the upper lip. Furthermore, because of the interrelationship between the developing face and forebrain, midline cleft, especially when premaxilla is absent, may indicate a sequence of associated facial and cerebral anomalies [26]. Since there is a close relationship between the cells of the neural crest and the closing neural tube, defects in these frontonasal process derivatives can lead to severe brain malformations.

Related anomalies associated with the incomplete development of fronto nasal process may include hemi-cephalus, holoprosencephaly and cyclopia. Therefore these gross anomalies may appear in tandem along with median cleft lip. Interestingly, midline diastemas of the maxillary dentition may appear as the mildest form of this anomaly [27].

Although various methods of classification of midline clefts of the face have been proposed, the most practical

divides midline clefts into two distinct groups [26, 28, 29]. In the first (DeMyer groups I through V), median cleft of the lip is typically associated with hypotelorism, holoprosencephaly, and agenesis of midline facial elements such as the premaxilla, nasal bones, and nasal septum. Orbital hypotelorism is present because of agenesis or hypoplasia of the ethmoid. Amentia is always present, and these patients rarely survive infancy. With the history of presence of facial dysmorphias in other family members, the possibility of recurrence in a subsequent child is as high as 50 % [30].

The second group (median cleft face syndrome) displays a much milder deformity, with a cleft lip that may be associated with varying mild degrees of nasal clefting and orbital hypertelorism. Occasionally, the corpus callosum is absent. However, intelligence and longevity are usually normal in this group. Therefore, patients with median cleft lip that fall into this category are candidates for early surgical repair.

The objectives of surgical repair are both aesthetic and functional. Aesthetic concerns involve narrowing the widened philtral column and alar bases, lengthening the columella, and restoring the normal contour of the tubercle. Function of the orbicularis oris is improved by resection of the amuscular component. Incision design should address removal or repositioning of abnormal labial frenum. Associated nasal deformities, which may range from mild notching to frank clefting, are also treated (Figs. 4, 5, 6, 7).

Fig. 4 Preoperative view of wide midline cleft lip

Fig. 5 Postoperative view of wide midline cleft lip

Various techniques like Francesconi triangular flap technique [31], Pinto and Goleria's modified Z-plasty [27] and inverted 'V' excision technique have been described. Repair of an existing shortened or widened columella may be incorporated into the repair [1, 32, 33]. Lengthening of the upper lip is achieved by increasing the length of the

Fig. 6 Preoperative view of mild midline notching

Fig. 7 Postoperative view of mild midline notching case

incision from lip vermillion border to columellar base at the expense of transverse lip length. Alternatively, a Z-incision may be added. Creation of a proper midline lip tubercle is important and needs adequate eversion of the vermillion [34].

Timing of surgical repair is consistent with that of other cleft lip deformities, the incision design should incorporate the principles previously mentioned, especially when concomitant local nasal deformities must be addressed.

Wide variation exists within this deformity, and each case must therefore be individually considered. The cases which were operated upon, showed good results keeping the following three major outcomes in mind: Excision of the tight, constrictive labial band; midline orbicularis oris muscle approximation; and an esthetically acceptable mucosal lengthening. Along with the above three major outcomes acceptable vermillion fullness was also achieved with an attempt to minimizing the post-operative cutaneous scar.

Conflict of interest None.

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